Lead Acetate Trihydrate

CAS #301-04-2
Swiss CD-1 mice, at 0.0, 0.5, 1.0, and 2.0% in water
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$Pb(C_2H_3O_2)_2 \cdot 3H_2O$

Lead acetate trihydrate (PbA) is used in manufacturing other lead salts, in the textile industry, and in veterinary medicine. It was tested for reproductive toxicity in Swiss CD-1 mice, using the RACB protocol (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). From data in the literature, levels of 0.5, 1.0, and 2.0% in water were selected for the continuous breeding phase of the study.

For the first generation (Task 2), mortalities were elevated at all doses. In controls animals, 3 males and 4 females (3M/4F) died, while in low, medium, and high doses, 0M/12F, 1M/16F, and 16M/17F died, respectively. This excessive mortality confounds the interpretation of the other data. In the low and middle dose groups, the deaths occurred late in Task 2, while the high dose deaths occurred throughout Task 2. The following number of pairs could still contribute data for Task 2: 36, 19, 10, and 4, from the control to high dose groups, respectively.

Reproductive toxicity was observable at all dose levels. The number of litters per pair was reduced by 29 and 58% in the middle and high dose groups. The number of live pups per litter was also reduced in medium and high doses (16 and 55%, respectively), while adjusted live pup weight was reduced in all groups by 4% (low), 12% (medium), and 16% (high). At the high dose, cumulative days to litter increased markedly for all litters. No high-dose pair produced a fifth litter.

Despite the excessive mortality, a Task 3 crossover study was performed to attempt to identify the more affected sex, using the control and 0.5% PbA mice. Pairs with a treated female delivered approximately 16% fewer pups per litter. Females in this group continued to die (3 of 9 died during this task).

After the Task 3 litters were delivered and evaluated the F_0 adult control and 0.5% PbA animals were killed and necropsied. Female body weight was unaffected, but brain weight was reduced by approximately 8%. The estrous cycle was unaffected in the 6 remaining females. Male body weight was unaffected by 0.5% PbA; organ weights did not differ between the groups nor did sperm measures.

Task 4, the F_2-generation assessment, only used offspring from the low dose group. Body weights and viability were not recorded during nursing. At the beginning of the cohabitation period for Task 4, body weights for treated mice were lower than controls by 12% (males) and 6% (females). There were sufficient mice to compose 14 control pairs and 16 treated pairs. The PbA-treated mice delivered 20% fewer live pups per litter, and those pups weighed approximately 7% less than their controls. Pup viability and sex ratio were unaffected by PbA exposure.

After the F_2 pups were evaluated and removed, the F_1 adults were killed and necropsied. Treated females weighed approximately 6% less than controls, while the pituitary weighed 35% less. Interestingly, the estrous cycle did not differ between the groups. For males, body weight was reduced by 12%, and absolute testis weight was 11% less than controls. Sperm measures did not differ between these two groups.

In conclusion, these concentrations of lead acetate trihydrate produced mortality and reproductive toxicity. A subsequent study at the other RACB laboratory used lower doses in an attempt to separate the potential reproductive/developmental toxicity of lead from the mortality induced by these concentrations.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85203032/AS**
Chemical: **Lead Acetate Trihydrate**
CAS#: **301-04-2**
Mode of exposure: **Water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.5%	1.0%	2.0%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	not necropsied	not necropsied
Kidney weight[a]	•, •	•, •	•, •
Liver weight[a]	—, —	•, •	•, •
Mortality	↑, ↑	↑, ↑	↑, ↑
Feed consumption	•, •	•, •	•, •
Water consumption	—, —	—, —	—, —
Clinical signs	—, —	—, —	↑, ↑
Reproductive toxicity			
x̄ litters/pair	—	↓	↓
# live pups/litter; pup wt./litter	—, ↓	↓, ↓	↓, ↓
Cumulative days to litter	—	—, —	↑
Absolute testis, epididymis weight[a]	—, —	•, •	•, •
Sex accessory gland weight[a] (prostate, seminal vesicle)	↓, —	•, •	•, •
Epidid. sperm parameters (#, motility, morphology)	—, —, —	•, •	•, •
Estrous cycle length	—	•, •	•, •

Determination of affected sex (crossover)	Male	Female	Both
Dose level	?	?	?

F_1 generation — Dose concentration →	0.5%	•	•
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•, •	•, •	•, •
Mortality	•, •	•, •	•, •
Adult body weight	↓, ↓	•, •	•, •
Kidney weight[a]	•, •	•, •	•, •
Liver weight[a]	—, —	•, •	•, •
Feed consumption	•, •	•, •	•, •
Water consumption	—, —	•, •	•, •
Clinical signs	—, —	•, •	•, •
Reproductive toxicity			
Fertility index	—	•	•
# live pups/litter; pup wt./litter	↓, ↓	•, •	•, •
Absolute testis, epididymis weight[a]	↓, —	•, •	•, •
Sex accessory gland weight[a] (prostate, seminal vesicle)	—, —	•, •	•, •
Epidid. sperm parameters (#, motility, morphology)	—, —, —	•, •, •	•, •, •
Estrous cycle length	—	•	•

Summary information	
Affected sex?	Female
Study confounders:	Significant mortality
NOAEL reproductive toxicity:	<0.5%
NOAEL general toxicity:	<0.5%
F_1 more sensitive than F_0?	Unknown
Postnatal toxicity:	Unknown

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.